REMARKS

Claims 1, 4, 14-16, 33 and 34 are pending in the present application.

Claims 1, 16, 33, and 34 have been amended. Claims 5-13, 17-32 and 35-38, inclusive, have been canceled.

I. Amended Claims 1, 16, 33, and 34.

Claims 1, 33 and 34 each have been amended to specify that the pharmaceutical composition, which is one component of the claimed article of manufacture, contains an amount of the specified nucleic acid sufficient to express an angiogenesis stimulating amount of the active Src protein in the tissue to which the nucleic acid is administered. Support for this amendment is found on page 21, line 15-19 and page 26, lines 23-31.

Claim 16 has been amended to correct an obvious grammatical error by substituting "a" for "an" before the word non-viral.

No new matter is added by any of these amendments.

II. Claims 1, 4, 14-16, 33 and 34 Do Not Contain New Matter

Claims 1, 4, 14-16, 33 and 34 were rejected for purportedly failing to comply with the written description requirement, as containing subject matter that was not described in the specification. According to the Office Action, the specification does not describe "an amount of a nucleic acid sufficient to deliver at least 0.1 grams of human Src protein per 100 grams of pharmaceutical compositions." Applicants disagree with that assessment of the specification; however, in the interest of advancing prosecution, the allegedly unsupported claim language has been replaced. The currently amended claims specify that the pharmaceutical composition contains an amount of the nucleic acid sufficient to express an angiogenesis stimulating amount of the active src protein in the tissue to which the nucleic acid is administered. The specification amply supports the language of the amended claims. Methods for measuring stimulation of angiogenesis are described in the specification, and are well known in the art. Accordingly, the determination of the precise dosage of nucleic acid to be included in the composition is well within the capability of those of ordinary skill in the art. Applicants deem this ground for rejection to be moot.

III. Claims 1, 4, and 16 are Patentable over Kato *et al.*

Claims 1, 4, and 16 stand rejected as being anticipated by Kato *et al.* as evidenced by the instruction manual for BioRad Gene Pulser. This rejection is unwarranted and should be withdrawn. The Office Action repeatedly characterizes these claims as *composition claims*, which they are not (see e.g., page 2, last paragraph of the Office Action). Claims 1, 4, and 16 are directed to articles of manufacture (i.e., kits), not to compositions.

The kits of the present claims must include the following components:

1. packaging material;

2. a pharmaceutical composition contained within the packaging material that is capable of stimulating angiogenesis, and which includes

(a) a nucleic acid encoding for an active human Src protein in an amount sufficient to deliver at least 0.1 of human Src protein per 100 grams of pharmaceutical composition, and

(b) pharmaceutically acceptable excipient or carrier; and

3. *a label containing specified printed matter* setting forth instructions and directions for use of the composition (i.e. instructions).

Anticipation requires the presence in a single prior art reference disclosure of each and every element of the claimed invention, arranged as in the claim. *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick,* 730 F.2d 1452, 1458, 221 USPQ 481, 485 (Fed. Cir. 1984). The Kato *et al.* reference does not teach or suggest all of the elements of the claims. This reference does not teach or suggest a kit containing a *packaged* pharmaceutical composition that includes *a nucleic acid* encoding for a human Src protein, *and a carrier* or excipient, as required by the claims, and further includes *a label* containing the specified instructions. Nor does this reference disclose the amount of the nucleic acid in the composition component of the kit as set forth in the claims. Furthermore, the BioRad manual does not teach or suggest the label requirements or the specified amount of nucleic acid set forth in the claims, either.

The Office Action indicates that printed words on a label cannot be given

patentable weight unless an intrinsic quality of the article is changed by the written matter, and cites to *In re Ngai* 70 USPQ2d 1862 to support this argument. *Ngai* is distinguishable on its facts from the present case. Applicants have set forth their position with respect to the printed matter on the label in several prior Responses. The inclusion of a label on the kit is a material requirement of the present claims. In claim 1, the printed matter on the label should be given patentable weight because the instructions and information on the label impart specific, new functionality to the article of manufacture that was previously unknown to one of ordinary skill in the art. The printed matter would have distinguished the claimed articles of manufacture from any other article containing such a composition, were such article to have been known in the art. Furthermore, the information on the label *vis-a-vis* the ability of active Src proteins to stimulate angiogenesis is novel and informs the user of the article how the article is to be utilized. *In re Miller*, 164 USPQ 46, 49 (CCPA 1969) and *In re Gulack*, 217 USPQ 401, 403 (CCPA 1983) support this position.

In re Ngai is distinguishable from the present case because the Patent Office argued, and Ngai conceded, that a *kit* comprising both a *composition* (a buffer) *and a set of instructions* as set forth in the disputed claim, was known in the prior art. That is not the case here. The Office Action does not point out, and Applicants do not find a disclosure of a *kit* comprising the nucleic acid composition *and a label* in the applied reference. In *Ngai*, both elements of the claim were disclosed in the reference. Here, the only elements of the claim disclosed in the applied reference is the nucleic acid in a carrier. The label, the specific instructions on the label, and the amount of nucleic acid in the nucleic acid composition are not disclosed by the references. As a matter of law, Kato *et al.* cannot anticipate the present claims, regardless of the teachings of the BioRad manual.

IV. Claims 1, 4, and 15 are Patentable over Tanaka *et al.*

Claim 1, 4, and 15 stand rejected as being anticipated by Tanaka *et al.* This rejection is unwarranted. As in the case of Kato *et al.*, the Tanaka *et al.* reference does not teach or suggest the specified nucleic acid, in the specified amount, in combination with a label. Accordingly, this reference cannot anticipate the present claims.

V. Claims 1, 14, and 15 are Patentable over Kato *et al.* in View of Boyse *et al.*

Claims 1, 14, and 15 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over Kato *et al.* in view of Boyse *et al.* In order to establish a *prima facie* case for obviousness, all claim limitations must be taught or suggested by the prior art. *In re Royka*, 180 USPQ 580 (CCPA 1974). That is not the case here. Additionally, "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 165 USPQ 494, 496 (CCPA 1970). It is black letter law that obviousness is determined at the time the invention was made. In the present case, one of ordinary skill in the art would not have been able to use the claimed articles of manufacture to stimulate angiogenesis, since this concept was unknown to one of ordinary skill in the art at the time the invention was made.

As noted above, Kato *et al.* does not teach or suggest the label limitation, the specific instructions on the label, or the amount of nucleic acid specified by the present claims. The combination of Kato *et al.* with Boyse *et al.* suffers from the same deficiencies. Boyse *et al.* merely discloses known techniques for inserting genes into cells; it does not teach or suggest the limitations of the claims that are absent from Kato *et al.* Accordingly, this combination of references would not have rendered the articles of manufacture of the present claims obvious to one of ordinary skill in the art at the time the invention was made.

VI. Claims 33 and 34 are Patentable over Kato *et al.* in View of Boyse *et al.* and GenBank Accession No. X59932.

Claims 33 and 34 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over Kato *et al.* in view of Boyse *et al.* and GenBank Accession No. X59932. The combination of these references would not have rendered claims 33 and 34 obvious to one of ordinary skill in the art.

Claims 33 and 34 are directed to pharmaceutical compositions for stimulating angiogenesis in a target tissue comprising a viral (claim 33) or non-viral (claim 34) gene transfer vector containing a nucleic acid and pharmaceutically acceptable carrier or excipient; said nucleic acid having a nucleic acid segment encoding for an active src protein having the amino acid residue sequence of SEQ ID NO: 5, wherein the pharmaceutical composition contains an

amount of said nucleic acid sufficient to express an angiogenesis stimulating amount of the Src protein in the tissue.

While GenBank Accession No. X59932 discloses a protein having the amino acid sequence of SEQ ID NO: 5, the combination of this reference with Kato *et al.* and Boyse *et al.* does not disclose the remaining limitations of the claims. This combination of references certainly would not have suggested to one of ordinary skill in the art at the time the invention was made the specific amount of nucleic acid present in the claimed compositions. Thus, the presently claimed composition would not have been obvious based on this combination of references.

VII. Conclusion

Claims 1, 4, 14, 15, 16, 33, and 34 are patentable over the applied art. Reconsideration and early passing of this application to issue is earnestly solicited.

Respectfully submitted,

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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this AMENDMENT AND RESPONSE UNDER RULE 111 is being transmitted by facsimile transmission to Fax No. 703-872-9306 on February 2, 2005.

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